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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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01/11/99 1:560 U.S. PTO

Complete if Known	
Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1616
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

Sheet 1 of 16

U.S. PATENT DOCUMENTS

Examiner's Initials*	Cite No.[1]	US Patent Document Number	~~Kind Code~~ [2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	~~Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear~~ Class / Subclass
KES	*	2,470,296		Fields	5/17/49	427/213.31
	*	2,533,065		Taplin, et al	3/8/47 D 50	424 497
	*	2,992,645		Fowler	7/18/61	128/203.21
		3,781,230		Vassiliades, et al	12/25/73	206/387.1
		3,957,965		Hartley, et al. 05	04/18/76	424/452
		4,009,280		Macarthur, et al.	02/22/77	514/456
		4,089,800		Temple 05	04/16/78	427/213.31
		4,161,516		Bell	07/17/79	424/451
		4,173,488		Vassiliades, et al.	11/06/79	106/216.1
		4,272,398		Jaffe	06/09/81	427/213.31
		4,352,883		Lim	10/05/82	435/178
		4,391,909		Lim	07/05/83	435/1.1
		4,466,442		Hilmann, et al.	08/21/84	600/431
		4,524,769		Wetterlin	06/25/85	128/203.15
		4,572,203		Feinstein	02/25/86	424/9.52
		4,590,206		Forrester, et al.	05/20/86	514/456
		4,615,697		Robinson	10/07/86	424/428
		4,679,555		Sackner	07/14/87	128/203.15
		4,741,872		De Luca, et al. 5	04/03/88	264/4.7
		4,743,545		Torobin	05/10/88	435/4
		4,774,958		Feinstein	10/04/88	424/9.52
		4,789,550		Hommel,, et al.	12/06/88	424/493
		4,818,542		DeLuca, et al.	04/04/89	424/491
		4,847,091		Illum	07/11/89	424/455
KES						

Examiner's Signature	Shelborne	Date Considered	6/14/99

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Sheet 2 of 16

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						424 / 487
KES		4,855,144		Leong, et al.	08/08/89	514 / 772.3
		4,857,311		Domb, et al.	08/15/89	427 / 213.31
		4,861,627		Mathiowitz, et al	08/29/89	264 / 122
		4,865,789		Castro, et al.	09/12/89	424 / 490
		4,904,479		Illum	02/27/90	131 / 273
		4,917,119		Potter, et al.	04/17/90	424 / 491
		4,976,968		Steiner	12/11/90	424 / 497
		4,994,281		Muranishi, et al.	02/19/91	128 / 203.21
		5,033,463		Cocozza	07/23/91	206 / 387.1
		5,064,065		Lew	11/12/91	427 / 213.33
		5,069,936		Yen	12/03/91	424 / 193.1
		5,075,109		Tice, et al.	12/24/91	424 / 426
		5,100,669		Hyon, et al.	03/31/92	600 / 431
		5,123,414		Unger	06/23/92	424 / 487
		5,160,745		DeLuca, et al.	11/03/92	521 / 64
		5,169,871		Hughes, et al.	12/08/92	600 / 438
		5,195,520		Schlief, et al.	03/23/93	424 / 434
		5,204,108		Illum	04/20/93	424 / 454
		5,204,113		Hartley, et al.	04/20/93	514 / 291
		5,260,306		Boardman, et al.	11/09/93	427 / 213.31
		5,271,961		Mathiowitz, et al.	12/21/93	128 / 203.12
		5,327,883		Williams, et al.	07/12/94	424 / 9.51
		5,334,381		Unger	08/02/94	424 / 9.51
KES		5,352,435		Unger	10/04/94	424 / 9.51

Examiner's Signature	Shelborne	Date Considered	6/14/99

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Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1616
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

Sheet 3 of 16

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KES		5,384,133		Boyes, et al.	01/24/95	341/22
		5,393,524		Quay	02/28/95	424/9.52
		5,407,609		Tice, et al.	04/18/95	264/4.6
		5,456,917		Wise, et al.	10/10/95	424/426
		5,478,578		Arnold, et al	12/26/95	424/499
		5,482,946		Clark, et al.	01/09/96	514/291
		5,518,709		Sutton, et al.	04/21/96	424/9.52
KES		5,607,695		Ek, et al.	03/04/97	424/468

FOREIGN PATENT DOCUMENTS

Examiner's Initials*	Cite No.[1]	Foreign Patent Document ~~Office[3]~~	Number[4]	~~Kind Code[5] (if known)~~ Country	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	~~Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear~~ Class/Subclass	T[6]
KES			0 072 048	EPA		02/16/83		
			0 213 303	EPA		06/23/86		
			0 257 915	EP		03/02/88		
			0 324 938	EPA		07/26/89		
			0 458 745	EPA		05/14/91		
			0 335 133	EP		10/04/89		
			1 288 583	GB		11/17/69		
			WO 80/02365	~~PCT~~ WO		11/13/80		
			WO 88/04556	~~PCT~~ WO		06/30/88		
			WO 88/09163	~~PCT~~ WO		12/01/88		
KES	-		WO 91/04732	~~PCT~~ WO		04/18/91		

Examiner's Signature	Shelbourne	Date Considered	6/14/99

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Complete if Known	
Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1615
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

Sheet 4 of 16

FOREIGN PATENT DOCUMENTS

Examiner's Initials*	Cite No.[1]	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	~~Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear~~ Class/Subclass	T[6]
		Office[3]	Number[4]	Kind Code[5] (if known)				
KES			WO 91/0627	~~PCT~~ WO		05/16/91		
			WO 91/06286	~~PCT~~ WO		05/16/91		
			WO 91/12823	~~PCT~~ WO		09/05/91		
			WO 92/18164	~~PCT~~ WO		10/29/92		
			WO 92/21382	~~PCT~~ WO		12/10/92		
			WO 93/25221	~~PCT~~ WO		12/23/93		
			WO 94/08627	~~PCT~~ WO		04/28/94		
			WO 94/16739	~~PCT~~ WO		04/04/94		
			WO 94/07514	~~PCT~~ WO		04/14/94		
			WO 95/00127	~~PCT~~ WO		01/05/95		
			WO 95/24183	~~PCT~~ WO		09/14/95		
			WO 95/07072	~~PCT~~ WO		03/16/95		
			WO 96/09814	~~PCT~~ WO		04/04/96		
			WO 96/15814	~~PCT~~ WO		05/30/96		
KES			WO 97/36574	~~PCT~~ WO		10/09/97		

Examiner's Signature	Shelborne	Date Considered	6/14/99

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01/11/99 U.S. PTO

Complete if Known	
Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1615
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

Sheet 5 of 16

OTHER ART -- NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cit and/or country where published	T[2]
KES		Adjei and Garren, "Pulmonary Delivery of Peptide Drugs: Effect of Particle Size on Bioavailability of Leuprolide Acetate in Healthy Male Volunteers," J. Pharm. Res., 7(6): 565-569 (1990).	
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		Brain, "Physiology and Pathophysiology of Pulmonary Macrophages," in The Reticuloendothelial System, Reichard and Filkins, Eds., Plenum Press, New York, pp. 315-327 (1985).	
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KES		Byron, "Determinants of drug and polypeptide bioavailability from aerosols delivered to the lung," Adv. Drug. Del. Rev., 5: 107-132 (1990)	

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Attorney Docket Number	MIT 7513/7804

Sheet 6 of 16

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KES		Carroll, et al. "Gelatin Encapsulated Nitrogen Microbubbles as Ultrasonic Contrast Agents" Investigative Radiology 15: 260-266 (1980).	
		Carroll, et al. "Ultrasonic Contrast Enhancement of Tissue by Encapsulated Microbubbles" Radiology 143:747-750 (1982).	
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Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

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		Davis, et al. "Polymeric microspheres as drug carries" Biomaterials 9:111-115 (1988).	
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		Dorries and Valberg, "Heterogeneity of phagocytosis for inhaled versus instilled material," Am. Rev. Resp. Disease, 146: 831-837 (1991).	
		* Doubrow, M., Ed., "Microcapsules and Nanoparticles in Medicine and Pharmacy," CRC Press, Boca Raton, (1992).	
		Edwards, et al. "Large Porous Particles for Pulmonary Drug Delivery" *Science*, 276: 1868-71 (1997).	
		Edwards, "The macrotransport of aerosol particles in the lung: Aerosol deposition phenomena," J. Aerosol Sci., 26: 293-317 (1995)	
		Eldridge et al., "Biodegradable microspheres as a vaccine delivery system," Mol. Immunol., 28: 287-294 (1991).	
		Feinstein, et al. "Two-Dimensional Contrast Echocardiography. I. In Vitro Development and Quantitative Analysis of Echo Contrast Agents" JACC 3(1): 14-20 (1984).	
		Ferin, "Pulmonary Retention of Ultrafine and Fine Particles in Rats" Am. J. Respir. Cell Mol. Biol. 6: 535-542 (1992).	
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Examiner's Signature	Shelborne	Date Considered	6/14/99

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Complete if Known	
Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1615
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

Sheet 8 of 16

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cit and/or country where published	T[2]
KES		French, Edwards, and Niven, "The influence of formulation on emission, deaggregation and deposition of dry powders for inhalation," J. Aerosol Sci., 27: 769-783 (1996).	
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		Gonda, "Physico-chemical principles in aerosol delivery," in Topics in Pharmaceutical Sciences 1991, Crommelin, D.J. and K.K. Midha, Eds., Medpharm Scientific Publishers, Stuttgart, pp. 95-117, 1992.	
		Gonda, "Targeting by deposition," in *Pharmaceutical Inhalation Aerosol Technology* (ed. A.J. Hickey), Marcel Dekkar Inc., New York, 1992.	
		Gurney, et al. Bioadhesive intraoral release systems: design, testing and analysis" Biomaterials 5: 336-340 (1984)	
		Heyder et al., "Deposition of Particles in the Human Respiratory Tract in the Size Range 0.005-15 micrometers," J. Aerosol Sci., 17: 811-825 (1986).	
KES		Heyder and Rudolf, "Mathematical models of particle deposition in the human respiratory tract," J. Aerosol Sci., 15:697-707 (1984).	

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Group Art Unit	1615
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		Hickey et al., "Use of particle morphology to influence the delivery of drugs from dry powder aerosols," J. Biopharmaceutical Sci., 2(1/2):107-113 (1992).	
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Group Art Unit	1616
Examiner Name	K. Shelbourne
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		Kricheldorf, H. R. *α-Aminoacid-N-Carboxy-Anhydrides and Related Heterocycles*, Springer-Verlag, Berlin, 1987.	
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	-	Lai, et al. "Protection Against Mycoplasma pulminosis Infection by Genetic Vaccination" DNA and Cell Biology 14(7): 643-651 (1995).	
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KES	-	Langer, "New Methods of Drug Delivery," Science, 249:1527-1533 (1990).	
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Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1615
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

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Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1616
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

Sheet 12 of 16

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KES		Menache, et al. "Particle Inhalability Curves for Humans and Small Laboratory Animals" Annals of Occupational Hygiene 39(3): 317-328 (1995).	
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		Smith, et al. "Aerosol Administration of Antibiotics" Respiration, 62(1) 19-24 (1995).	
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KES		* Tansey, "The challenges in the development of metered dose inhalation aerosols using ozone-friendly propellants," Spray Technol. Market, 4:26-29 (1994).	

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KES		Timsina et al., "Drug delivery to the respiratory tract using dry powder inhalers," Int. J. Pharm., 101: 1-13 (1994).	
		Turner, J. and S. Hering, "Greased and oiled substrates as bounce-free impaction surfaces," J. Aerosol Sci., 18: 215-224 (1987).	
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		Wichert, et al. Low molecular weight PLA: a suitable polymer for pulmonary administered microparticles?" J. Microencapsulation, 10: 195-207 (1993).	
		Wong and Suslick, "Sonochemically produced hemoglobin microbubbles," Mat. Res. Soc. Symp. Proc., 372:89-95 (1995).	
KES		Zanen et al., "The optimal particle size for β-adrenergic aerosols in mild asthmatics," Int. J. Pharm., 107: 211-217 (1994).	
Examiner's Signature	Shelbourne		6/14/99

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Complete if Known	
Application Number	08/971,791
Filing Date	November 17, 1997
First Named Inventor	David A Edwards
Group Art Unit	1615
Examiner Name	K. Shelbourne
Attorney Docket Number	MIT 7513/7804

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KES		Zanen et al., "The optimal particle size for parasympathicolytic aerosols in mild asthmatics" Int. J. Pharm., 114:111-115 (1995).	
1		Zeng, et al. "Tetrandrine delivery to the lung: The optimisation of albumin microsphere preparation by central composite design" Int. J. Pharm., 109: 135-145 (1994).	
KES		Zeng et al., "The controlled delivery of drugs to the lung," Int. J. Pharm., 124:149-164 (1995).	
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